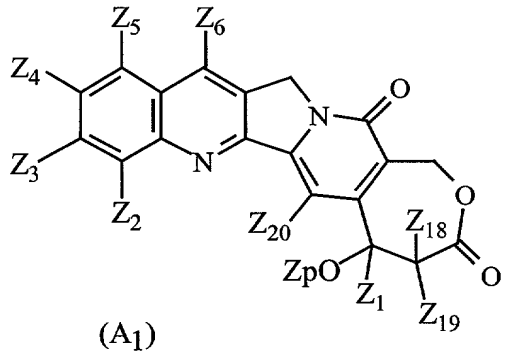
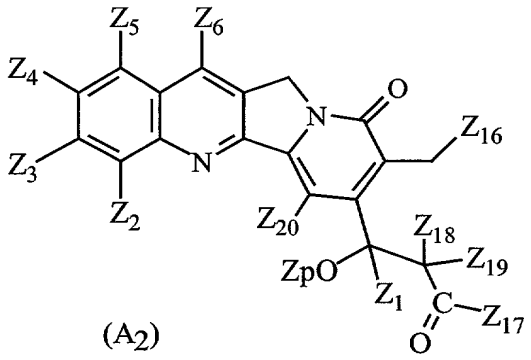
CLAIMS

1. Compounds of general formula (A_1) or (A_2)



(A_1)



(A_2)

in racemic or enantiomeric form or any combinations of these forms, in which

Z_1 represents a lower alkyl, a lower alkenyl, a lower alkynyl, a lower haloalkyl, a lower alkoxy lower alkyl or lower alkylthio lower alkyl;

Z_2, Z_3, Z_4, Z_5 and Z_6 represent, independently,

i) H, halo, lower haloalkyl, alkyl containing 1 to 12 carbon atoms optionnally substituted by one or more halo radicals indentical or different, lower alkenyl, cycloalkyl, cycloalkyl lower alkyl, cyano, lower cyanoalkyl, nitro, lower nitroalkyl, amido, lower amidoalkyl, hydrazino, lower hydrazinoalkyl, azido, lower azidoalkyl, lower alkyl lower sulphonylalkyl, $-(CH_2)_mNZ'_6Z'_7$, $-(CH_2)_mOZ'_6$, $-(CH_2)_mSZ'_6$, $-(CH_2)_mCO_2Z'_6$, $-(CH_2)_mNZ'_6C(O)Z_8$, $-(CH_2)_mC(O)Z_8$, $-(CH_2)_mOC(O)Z_8$, $-O(CH_2)_mNZ'_6Z'_7$, $-OC(O)NZ'_6Z'_7$, $-OC(O)(CH_2)_mCO_2Z'_6$, $-OSO_2Z_7$, $-(CH_2)_mN(CH_3)(CH_2)_nNZ'_6Z'_7$, $-(CH_2)_mOC(O)NZ'_6Z'_7$, $-(CH_2)_mS(O)_qZ_{11}$, $-(CH_2)_mP(O)Z_{12}Z_{13}$, $-(CH_2)_2P(S)Z_{12}Z_{13}$, $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$; or **ii)** $-(CH_2)_n[N=X]$, $-OC(O)[N=X]$, $-(CH_2)_mOC(O)[N=X]$, aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group or the heterocycle) or non substituted in which the substituent is a lower alkyl, lower arylalkyl, halo, hydroxy, $-OCF_3$, nitro, amino, lower alkylamino, di(lower alkyl)amino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl or **iii)** Z_3 and Z_4 or Z_4 and Z_5 form together a chain with 3 or 4 members in which the elements of the chain are selected from the group constituted by CH, CH_2, O, S, N or NZ_9;

Z_7 represents a lower alkyl radical optionnally substituted by one or more halo radicals identical or different, or an aryl optionnally susbtituted by one or more lower alkyl radicals identical or different ;

Z'_6 and Z'_7 represent, independently, **i)** H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or **ii)** aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl ;

Z_8 represents **i)** H, a lower alkyl, lower hydroxyalkyl, amino, lower alkylamino, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy lower alkyl, lower haloalkyl, or **ii)** aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted, in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;

Z_9 represents **i)** H, a lower alkyl, lower haloalkyl, or **ii)** aryl or lower arylalkyl, each substituted or non substitutued in which the substituent is lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;

Z_{10} represents **i)** H, a lower alkyl, lower haloalkyl, lower alkoxy, or **ii)** aryl substituted (i.e. having one to four substituents on the aryl group)or non substituted in which the substitutent is lower alkyl, lower haloalkyl, lower hydroxyalkyl or lower alkoxy lower alkyl;

Z_{11} represents a lower alkyl, aryl, $-(CH_2)_mOZ_{14}$, $-(CH_2)_mSZ_{14}$, $-(CH_2)_2NZ_{14}Z_{15}$ or $-(CH_2)_m[N=X]$;

Z_{12} and Z_{13} represent, independently, a lower alkyl, aryl, lower alkoxy, aryloxy or amino;

Z'_{11}, Z'_{12} and Z'_{13} represent, independently, H or a lower alkyl radical ;

Z_{14} and Z_{15} represent, independently, H, lower alkyl or aryl;

Z_{16} represents H or $-OZ_{21}$;

Z_{17} represents $-OZ'_6$ or $-NZ'_6Z'_7$;

Z_{18} and Z_{19} represent, independently, H, halo, lower alkyl, lower alkoxy or hydroxy;

Z_{20} represents H or halo;

Z_{21} represents H, a lower alkyl, -CHO or $-C(O)(CH_2)_mCH_3$;

Z_p represents H or an easily cleavable group preferably chosen from the groups corresponding to the formula $-C(O)-A-NZ_{22}Z_{23}$, in which A represents a linear or branched alkylene radical optionally substituted by a radical chosen from the free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino, mono or dialkylamino radicals ;

Z_{22} and Z_{23} represent, independently, H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or substituted or non substituted aryl or lower arylalkyl (i.e., substituted one to four times on the aryl group), in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;

m is an integer comprised between 0 and 6;

n is 1 or 2; and

q represents an integer from 0 to 2; and

[N=X] represents a heterocyclic group with 4 to 7 members with the nitrogen atom which is a member of the heterocyclic ring, and X representing the chain necessary to complete said heterocyclic group and selected from the group constituted by O, S, CH_2, CH, N, NZ_9 and $C(O)Z_{10}$;

or pharmaceutically acceptable salts of thereof.

2. Compounds of general formula (A_1) or (A_2) as claimed in claim 1, in racemic or enantiomeric form or any combinations of these forms, characterized in that

Z_1 represents a lower alkyl, a lower alkenyl, a lower alkynyl, a lower haloalkyl, a lower alkoxy lower alkyl or lower alkylthio lower alkyl;

Z_2 represents H, halo or $-OSO_2Z_7$;

Z_3, Z_4 and Z_5 represent, independently, **i)** H, halo, lower haloalkyl, lower alkyl, lower alkenyl, cyano, lower cyanoalkyl, nitro, lower nitroalkyl, amido, lower amidoalkyl, hydrazino, lower hydrazinoalkyl, azido, lower azidoalkyl, $-(CH_2)_mNZ'_6Z'_7$, $-(CH_2)_mOZ'_6$, $-(CH_2)_mSZ'_6$, $-(CH_2)_mCO_2Z'_6$, $-(CH_2)_mNZ'_6C(O)Z_8$, $-(CH_2)_mC(O)Z_8$, $-(CH_2)_mOC(O)Z_8$, $-O(CH_2)_mNZ'_6Z'_7$, $-OC(O)NZ'_6Z'_7$, $-OC(O)(CH_2)_mCO_2Z'_6$, $-OSO_2Z_7$ or **ii)** $-(CH_2)_n[N=X]$, $-OC(O)[N=X]$, $-(CH_2)_mOC(O)[N=X]$ (in which [N=X], in this invention, represents a heterocyclic group with 4 to 7 members with the nitrogen atom N, which is a member of the heterocyclic group, and X represents the remaining members, which are

necessary to complete the heterocylic group, selected from the group constituted by O, S, CH_2, CH, N, NZ_9 and COZ_{10}), aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group or the heterocycle) or non substituted in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl or **iii)** Z_3 and Z_4 or Z_4 and Z_5 form together a chain with 3 or 4 members in which the elements of the chain are selected from the group constituted by CH, CH_2, O, S, N or NZ_9;

Z_6 represents **i)** H, halo, lower haloalkyl, alkyl containing 1 to 12 carbon atoms optionnally substituted by one or more halo radicals indentical or different, lower alkoxy, lower alkoxy lower alkyl, lower alkylthio lower alkyl, cycloalkyl, cycloalkyl lower alkyl, cyano, cyanoalkyl, lower alkyl lower sulphonylalkyl, lower hydroxyalkyl, nitro, $-(CH_2)_mC(O)Z_8$, $-(CH_2)_mNZ'_6C(O)Z_8$, $-(CH_2)_mNZ'_6Z'_7$, $-(CH_2)_mN(CH_3)(CH_2)_nNZ'_6Z'_7$, $-(CH_2)_mOC(O)Z_8$, $-(CH_2)_mOC(O)NZ'_6Z'_7$, $-(CH_2)_mS(O)_qZ_{11}$, $-(CH_2)_mP(O)Z_{12}Z_{13}$, $-(CH_2)_2P(S)Z_{12}Z_{13}$, $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$; or **ii)** $-(CH_2)_n[N=X]$, $-OC(O)[N=X]$, $-(CH_2)_mOC(O)[N=X]$, each substituted (i.e. substituted between once and four times on the heteroaryl group) or non substituted in which the substituent is a lower alkyl, lower arylalkyl, halo, hydroxy, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl; or **iii)** aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted in which the substituent is a lower alkyl, halo, hydroxy, nitro, $-OCF_3$, amino, lower alkylamino, di(lower alkyl)amino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl ;

Z_7 represents a lower alkyl radical optionnally substituted by one or more halo radicals identical or different, or an aryl optionnally susbtituted by one or more lower alkyl radicals identical or different ;

Z'_6 and Z'_7 represent, independently, **i)** H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or **ii)** aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl ;

Z_8 represents **i)** H, a lower alkyl, lower hydroxyalkyl, amino, lower alkylamino, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy lower alkyl, lower haloalkyl, or **ii)** aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted, in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;

Z_9 represents **i)** H, a lower alkyl, lower haloalkyl, or **ii)** aryl or lower arylalkyl, each substituted or non substitutued in which the substituent is lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;

Z_{10} represents **i)** H, a lower alkyl, lower haloalkyl, lower alkoxy, or **ii)** aryl substituted (i.e. having one to four substituents on the aryl group)or non substituted in which the substitutent is lower alkyl, lower haloalkyl, lower hydroxyalkyl or lower alkoxy lower alkyl;

Z_{11} represents a lower alkyl, aryl, $-(CH_2)_mOZ_{14}$, $-(CH_2)_mSZ_{14}$, $-(CH_2)_2NZ_{14}Z_{15}$ or $-(CH_2)_m[N=X]$;

Z_{12} and Z_{13} represent, independently, a lower alkyl, aryl, lower alkoxy, aryloxy or amino;

Z'_{11}, Z'_{12} and Z'_{13} represent, independently, H or a lower alkyl radical ;

Z_{14} and Z_{15} represent, independently, H, lower alkyl or aryl;

Z_{16} represents H or $-OZ_{21}$;

Z_{17} represents $-OZ'_6$ or $-NZ'_6Z'_7$;

Z_{18} and Z_{19} represent, independently, H, halo, lower alkyl, lower alkoxy or hydroxy;

Z_{20} represents H or halo;

Z_{21} represents H, a lower alkyl, -CHO or $-C(O)(CH_2)_mCH_3$;

Z_p represents H or an easily cleavable group preferably chosen from the groups corresponding to the formula $-C(O)-A-NZ_{22}Z_{23}$, in which A represents a linear or branched alkylene radical optionally substituted by a radical chosen from the free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino, mono or dialkylamino radicals ;

Z_{22} and Z_{23} represent, independently, H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or substituted or non substituted aryl or lower arylalkyl (i.e., substituted

one to four times on the aryl group), in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;

m is an integer comprised between 0 and 6;

n is 1 or 2; and

q represents an integer from 0 to 2; and

[N=X] represents a heterocyclic group with 4 to 7 members with the nitrogen atom which is a member of the heterocyclic ring, and X representing the chain necessary to complete said heterocyclic group and selected from the group constituted by O, S, CH_2, CH, N, NZ_9 and COZ_{10} ;

or pharmaceutically acceptable salts of thereof.

3. Compounds as claimed in claim 1 or 2, characterized in that Z_2 represents H or halo ; or pharmaceutically acceptable salts of thereof.

4. Compounds as claimed in claim 1 or 2, characterized in that Z_3 represents halo ; or pharmaceutically acceptable salts of thereof.

5. Compounds as claimed in any of claims 1 to 4, characterized in that

Z_1 represents a lower alkyl ;

Z_2 represents H or halo ;

Z_3, Z_4 and Z_5 represent, independently, **i)** H, halo, lower alkyl, $-(CH_2)_mNZ'_6Z'_7$, $-(CH_2)_mOZ'_6$, $-OSO_2Z_7$ or **ii)** $-(CH_2)_n[N=X]$ or **iii)** Z_3 and Z_4 or Z_4 and Z_5 form together a chain with 3 or 4 members in which the elements of the chain are selected from the group constituted by CH, CH_2, O, S, N or NZ_9;

Z_6 represents **i)** H, halo, alkyl containing 1 to 12 carbon atoms optionnally substituted by one or more halo radicals indentical or different, lower alkoxy lower alkyl, cycloalkyl, cycloalkyl lower alkyl, lower hydroxyalkyl, $-(CH_2)_mNZ'_6Z'_7$, $-(CH_2)mSiZ'_{11}Z'_{12}Z'_{13}$; or **ii)** $-(CH_2)_n[N=X]$ substituted or non substituted in which the substituent is a lower alkyl or lower arylalkyl or **iii)** aryl or lower arylalkyl, each substituted or non substituted in which the substituent is a lower alkyl, halo, $-OCF_3$, di(lower alkyl)amino or lower haloalkyl ;

Z_7 represents a lower alkyl radical optionnally substituted by one or more halo radicals identical or different ;

Z'_6 and Z'_7 represent, independently, **i)** H, a lower alkyl, or **ii)** lower arylalkyl ;

Z_9 represents a lower alkyl or lower arylalkyl ;

Z'_{11}, Z'_{12} and Z'_{13} represent, independently, a lower alkyl radical ;

Z_{16}	represents H or $-OZ_{21}$;
Z_{17}	represents $-OZ'_6$ or $-NZ'_6Z'_7$;
Z_{18} and Z_{19}	represent, independently, H, halo ;
Z_{20}	represents H ;
Z_{21}	represents H, a lower alkyl or $-C(O)(CH_2)_mCH_3$;
Z_p	represents H or a group corresponding to the formula -C(O)-A-$NZ_{22}Z_{23}$, in which A represents a linear or branched alkylene radical optionally substituted by a radical chosen from the free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino, mono or dialkylamino radicals ;
Z_{22} and Z_{23}	represent, independently, H, a lower alkyl ;
m	is an integer comprised between 0 and 6;
n	is 1 or 2; and
q	represents an integer from 0 to 2; and
[N=X]	represents a heterocyclic group with 4 to 7 members, X representing the chain necessary to complete said heterocyclic group and selected from the group constituted by O, CH_2, CH, N and NZ_9 ;

or pharmaceutically acceptable salts of thereof.

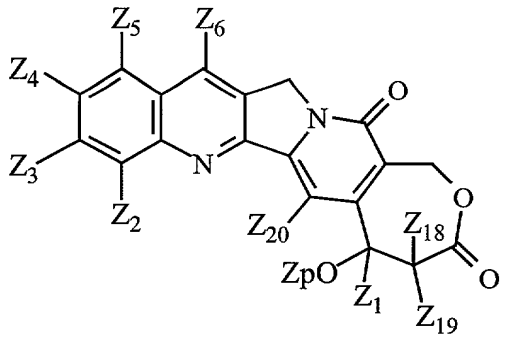
6. Compounds as claimed in any of claims 1 to 5, characterized in that Z_{18}, Z_{19} and Z_{20} represent H ; or pharmaceutically acceptable salts of thereof.

7. Compounds as claimed in any of claims 1 to 6, characterized in that Z_1 represents ethyl ; or pharmaceutically acceptable salts of thereof.

8. Compounds as claimed in claim 1 or 2, characterized in that Z_p represents a group corresponding to the formula -C(O)-A-$NZ_{22}Z_{23}$; or pharmaceutically acceptable salts of thereof.

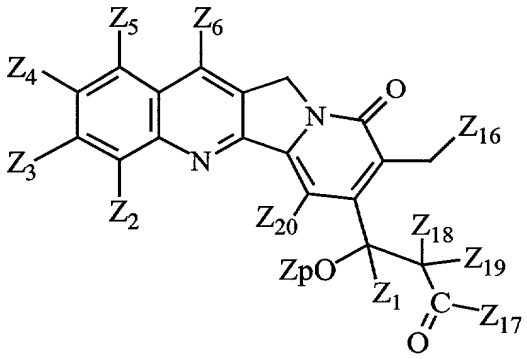
9. Compounds as claimed in claim 1 or 2, characterized in that Z_p represents H ; or pharmaceutically acceptable salts of thereof.

10. Compounds as claimed in claim 1 or 2, characterized in that they correspond to the formula (A1)



wherein Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_{18}, Z_{19}, Z_{20} and Z_p are as defined in claim 1 ; or pharmaceutically acceptable salts of thereof.

11. Compounds as claimed in claim 1 or 2, characterized in that they correspond to the formula (A2)



wherein Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_{16}, Z_{17}, Z_{18}, Z_{19}, Z_{20} and Z_p are as defined in claim 1 ; or pharmaceutically acceptable salts of thereof.

12. Compounds as claimed in claim 1 or 2, characterized in that Z_6 represents $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$; or pharmaceutically acceptable salts of thereof.

13. Compounds as claimed in claim 12, characterized in that they correspond to the following formula :

(5*R*)-5-ethyl-9,10-difluoro-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino[3',4':6,7]indolizino [1,2-*b*] quinoline-3,15-dione ;

(5*R*)-5-ethyl-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino [1,2-*b*] quinoline-3,15-dione ;

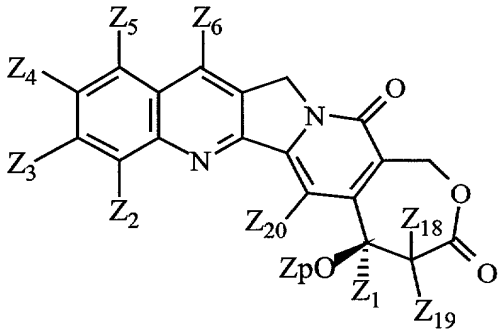
14. Compounds as claimed in claim 1 or 2, characterized in that Z_2 represents H or halo, Z_3 represents halo, Z_4 represents H, halo or lower alkyl, Z_5 represents H or halo, and Z_6 represents H, lower alkyl or $-(CH_2)_n[N=X]$ substituted in which the substituent is a lower alkyl ; or pharmaceutically acceptable salts of thereof.

15. Compounds as claimed in claim 14, characterized in that they correspond to the following formula :

(*5R*)-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ;

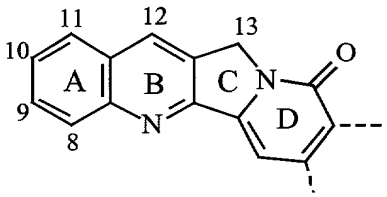
(*5R*)-5-ethyl-9,11-difluoro-5-hydroxy-12-propyl-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ; or pharmaceutically acceptable salts of thereof.

16. Compounds as claimed in claim 1 or 2, characterized in that they correspond to the formula

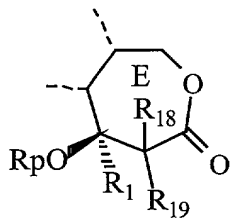


wherein Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_{18}, Z_{19}, Z_{20} and Z_p are as defined in claim 1 ; or pharmaceutically acceptable salts of thereof.

17. A method of treating cancer in warm-blooded animals comprising administering to warm-blooded animals in need thereof a camptothecin analog characterized in that said analog is a [A,B,C,D,E] pentacyclic compound, the cycles [A,B,C,D]



comprising any substitution on the various sites available for substitution(s), and the [E] cycle being a 7-ring member ß-hydroxy lactone ring of the formula



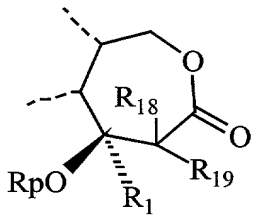
wherein R_1 is selected from the group consisting of alkyl of 1 to 6 carbon atoms, alkenyl and alkynyl of 2 to 6 carbon atoms, haloalkyl of 1 to 6 carbon atoms, alkoxyalkyl of 2 to 12 carbon atoms and alkylthioalkyl of 2 to 12 carbon atoms, R_p is hydrogen or an easily cleavable group, R_{18} and R_{19} are individually selected from the group consisting of hydrogen, halogen, OH and alkyl and alkoxy of 1 to 6 carbon atoms and its non-toxic, pharmaceutically acceptable salts.

18. A method of treating cancer according to claim 17, the cycles [A,B,C,D] comprising any substitution on the sites 8, 9, 10, 11, 12 or 13.

19. A method of treating cancer according to claim 17, the cycles [A,B,C,D] comprising any substitution on the sites 8, 9, 10, 11 or 12.

20. A method of treating cancer according to claim 17, the cycles [A,B,C,D] comprising any substitution on the sites 9, 10, 11 or 12.

21. A method of treating cancer in warm-blooded animals comprising administering to warm-blooded animals in need thereof a camptothecin having 5 rings with a 7-ring member ß-hydroxy lactone ring of the formula



wherein R_1 is selected from the group consisting of alkyl of 1 to 6 carbon atoms, alkenyl and alkynyl of 2 to 6 carbon atoms, haloalkyl of 1 to 6 carbon atoms, alkoxy alkyl of 2 to 12 carbon atoms and alkylthioalkyl of 2 to 12 carbon atoms, R_p is hydrogen or an easily cleavable group, R_{18} and R_{19} are individually selected from the group consisting of hydrogen, halogen, OH and alkyl and alkoxy of 1 to 6 carbon atoms and its non-toxic, pharmaceutically acceptable salts.

22. A method of treating cancer as claimed in claim 17 or 21, characterized in that cancer is selected from the group consisting of leukemia, colon cancer, lung cancer, prostate cancer, breast cancer, melanoma, ovarian cancer and gastric cancer.

23. A method of treating cancer as claimed in claim 22, characterized in that cancer is selected from the group consisting of leukemia, colon cancer, lung cancer, prostate cancer and breast cancer.

24. A method as claimed in any of claims 17 to 23 characterized in that R_{18} and R_{19} are hydrogen.

25. A method as claimed in any of claims 17 to 24 characterized in that R_p is hydrogen.

26. A method as claimed in any of claims 17 to 25 characterized in that R_1 is ethyl.

27. A method as claimed in any of claims 17 to 26 characterized in that camptothecin analog is selected from :

(*5R*)-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ;

(*5R*)-1-[9-chloro-5-ethyl-5-hydroxy-10-methyl-3,15-dioxo-4,5,13,15-tetrahydro - 1H,3H-oxepino [3',4:6,7] indolizino [1,2-b] quinolin-12-yl-methyl]-4-methyl-hexahydropyridium chloride ;

(*5R*)-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ;

(*5R*)-5-ethyl-9,11-difluoro-5-hydroxy-12-propyl-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ; or its pharmaceutically acceptable salts thereof.